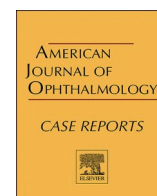




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Cataracts in setting of multisystem inflammation after COVID-19 vaccination

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ABSTRACT

Purpose: To describe a unique case of bilateral cataract formation in the setting of multisystem inflammation after the 1st dose of the BNT162b2 mRNA COVID-19 vaccination.

Observations: A previously healthy 20-year-old male developed intumescent bilateral cataracts leading to visual decline from 20/20 to 20/300–20/400 in each eye, likely from systemic inflammation after vaccination.

Conclusion and importance: This is the first reported case of cataract formation following a COVID-19 vaccine. While ocular adverse effects associated with COVID-19 vaccination are rare, it is important to raise awareness of these entities amongst medical providers as the COVID-19 pandemic continues and vaccinations become widespread.

1. Introduction

To combat the global coronavirus disease 2019 (COVID-19) pandemic, numerous COVID-19 vaccines were developed and received emergency approval by the U.S. Food and Drug Administration. While the Pfizer-BioNTech BNT162b2 mRNA vaccine has shown an extremely favorable safety profile with high efficacy, rare ocular effects have been reported. We describe a unique case of rapid formation of cataracts in an otherwise healthy patient in the setting of multisystem inflammation following the first dose of the BNT162b2 COVID-19 vaccine.

2. Case report

In April of 2021, a 20-year-old male college student with no medical history presented to the emergency department for evaluation of new-onset nausea, emesis, myalgias, abdominal pain, hematuria, and a diffuse pustular rash two days after receiving the first dose of the BNT162b2 COVID-19 vaccine.

At the time of presentation, he endorsed new bilateral eye redness and mild blurriness that began that day. His exam was notable for a pustular rash on his face and torso and VA of 20/20, mild conjunctival chemosis and trace follicular reaction in both eyes. His initial laboratory evaluation showed leukocytosis and acute kidney injury for which he was admitted.

He was started on empiric steroids for a presumed inflammatory reaction related to the mRNA COVID-19 vaccination. On day two, ophthalmic exam revealed resolving chemosis and conjunctivitis with resolution of subjective blurriness. Artificial tears as needed for comfort were recommended.

Two weeks later, patient began to experience bilateral blurriness worse at distance. His visual acuity was J1+ bilaterally and slit lamp exam revealed bilateral mild anterior and posterior subcapsular lens opacities radiating centrally. By this time, his hospital course had been complicated by numerous systemic events felt to be related to a vaccination-related hyper-inflammatory state, including pericarditis with cardiac tamponade requiring pericardiocentesis, pulmonary capillary leak, bilateral sensorineural hearing loss, and bilateral ischemic cerebellar cerebral vascular accidents. He was treated with two rounds of IVIG and pulse-dose steroids for three days and slowly tapered. While steroids were risk factors for cataract development, they were continued as the benefits of systemic immunosuppression outweighed the visual risks.

His cataracts continued to progress during admission while on a slow steroid taper. At month 3, his best corrected VA was 20/300 in the right eye and 20/400 in the left eye, lenses were intumescent with dense opacities radiating from the center and multiple scattered punctate opacities (Fig. 1A and B). OCT RNFL and macula were normal. During his hospital course, he remained without anterior chamber cells, high

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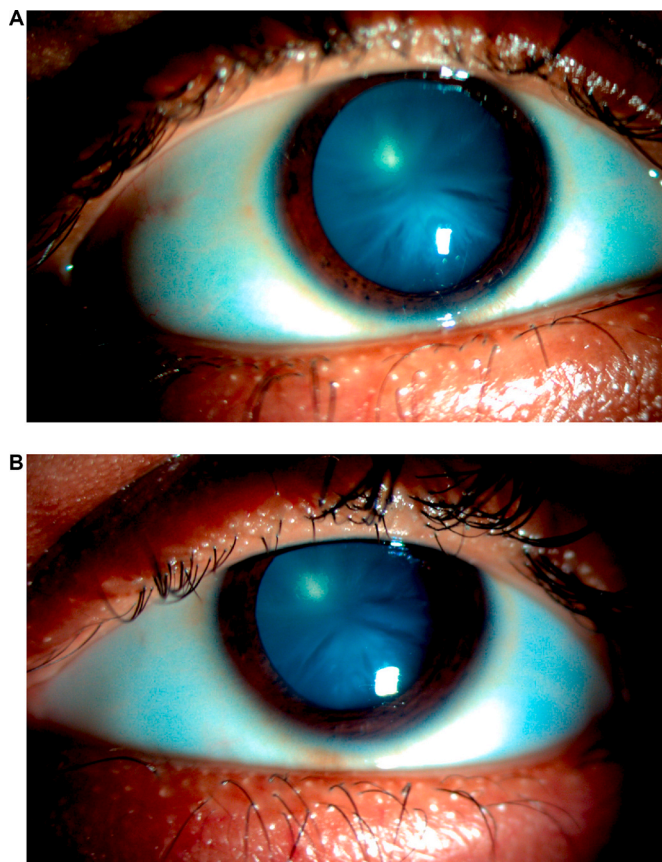


Fig. 1. Slit lamp photograph of cataracts of the right eye (1A) and left eye (1B) taken at 3 months after vaccination demonstrating dense anterior and posterior subcapsular lens opacities radiating from the center.

intraocular pressure, vitreous cells, disc edema, and other signs of inflammatory findings.

Given the visual significance and continued progression of cataracts, cataract extraction with phacoemulsification with an intraocular multifocal lens implantation was performed bilaterally two weeks apart. At post-op month 1, each eye had best corrected visual acuity 20/25.

Patient was transferred to inpatient rehabilitation after month 3 to focus on regaining functional mobility.

Laboratory diagnostic evaluation was performed during admission was notable for a systemic dysregulated inflammatory process, including elevated C-reactive protein, erythrocyte sedimentation rate, lactate dehydrogenase, and lymphopenia. Evaluation for malignancy was negative. He had a negative serum COVID-19 IgG and multiple negative COVID-19 PCR tests during admission, which ruled out a prior COVID-19 infection. He was negative for all other infectious work-up. Extensive autoimmune and genetic panel was notable for elevated IL-2, IL-10, IL-13, IL-6, and C-X-C Motif Chemokine Ligand 9 (CXCL9). He was negative for all other autoimmune markers including antinuclear antibodies, anticardiolipin antibody, antineutrophil cytoplasmic antibodies, anti-scl-70 antibodies, rheumatoid factor, SS-A antibodies, and SS-B antibodies.

3. Discussion

Since December 2020, several COVID-19 vaccines have been developed and approved for use around the world. Currently, the United States FDA has only approved two mRNA vaccines, the BNT162b2 and mRNA-1273 vaccines, which utilize purified, single-stranded RNA with nucleotide modifications to drive a mild type-1 IFN innate immune response and generate adaptive immunity. While these vaccines have an

overall excellent safety profile, rare ophthalmic manifestations have been reported by ophthalmologists.^{1,2} Most frequently reported complications are in the cornea, uvea, retina, and vasculature,^{3–10} possibly due to the ocular tropism of COVID-19 due to the anatomical and cellular similarities between the ocular and respiratory systems.^{11,12} However, to our knowledge, this is the first reported case of cataract development immediately after COVID-19 vaccination.

Multisystem inflammatory syndrome has been reported with COVID-19 infection and vaccination in adults.^{13,14} Given the patient's lack of comorbid conditions and unrevealing, extensive workup for his hyper-inflammatory state by a multidisciplinary medical team, we strongly suspect this patient to have a rare case of multisystem inflammatory syndrome-vaccine (MIS-V), as coined by Nune et al.¹⁴ Furthermore, despite clinical and laboratory improvements, he continued to have elevated levels of CXCL9, a chemokine specifically induced by IFN-gamma, suggestive of an interferonopathy that predisposes him to massive inflammatory responses.^{15,16}

While osmotic stress in diabetes and uncontrolled sustained hyperglycemia has been reported to contribute to acute cataract formation, this patient did not have diabetes and had normal blood sugars.¹⁷ Oxidative stress is another known factor in cataract formation, but typically takes months to years to take effect.¹⁸ Trauma is another risk factor for cataracts, but patient had no prior history of this.

Thus, we believe the most compelling etiology of his cataracts is the significant inflammatory dysregulation given their rapid onset after a recent, unremarkable ophthalmologic exam. While steroids were administered, they are highly unlikely to be a major contributing factor since steroid-induced cataracts develop over multiple years of consistent treatment.^{19,20}

Although many inflammatory diseases, such as Behcet's disease, are well known to cause cataracts, the mechanism underlying inflammation-induced cataracts is not well understood. In one study, Behcet cataract patients had significantly elevated IL-6 aqueous humor levels while Vogt-Koyanagi-Harada cataract patients had both significantly elevated IL-6 and IFN-gamma levels in the aqueous humor in comparison to patients with age-related cataracts.²¹ Similarly, while age-related cataracts are not deemed inflammatory in nature, age-related cataract patients have been found to have high levels of intraocular IL-23, implying that some underlying intraocular inflammatory pathway is activated and could potentially be driving cataract pathogenesis.²² Furthermore, animal studies have shown fibrotic changes in anterior subcapsular cataract formation can be mimicked after exposure to transforming growth factor- β alone,²³ suggesting abnormal cytokine levels could drive or accelerate cataract formation. As a reminder, this patient had persistently elevated levels of IL-6 and CXCL9, which lends itself to the theory that these inflammatory markers could have been elevated within the eye and driven accelerated cataract formation.¹⁶

4. Conclusions

To our knowledge, this is the first reported case of cataract formation in a previously healthy patient following the BNT162b2 COVID-19 vaccine. While ocular adverse effects associated with vaccination is rare, it is important for providers recognize these adverse effects as the COVID-19 pandemic continues and vaccinations become widespread.

Patient consent

Written informed consent for publication of the case was obtained from the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

All authors have no financial disclosures.

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